

Appl. No. 09/631,339
Reply to Final Office Action of Aug. 24, 2005

REMARKS

Applicants have submitted amendments to the claims that are believed to place the application in condition for allowance. Rejected claims 7, 8 and 16 have been canceled. Claims 1 and 21 have been amended to specify that the container consists of the listed elements. Claim 21 is further amended to incorporate the limitations of previously submitted claim 22 to state the thickness of the capillary tube walls. Claims 2, 3 and 11 are amended to clarify the claim language, and claims 9, 10 and 15 have been amended so that claims 9, 10-12 and 15 now depend from claim 1. Claim 4 has been amended to place it independent form, incorporating all the limitations of amended claim 1 and further specifying the presence of a third element, a stopper. Applicants acknowledge that these amendments are being made after final rejection and that entry of amendments after final are made at the Examiner's discretion. The amendments to the claims are believed to be responsive to the Examiner's most recent rejections in the present Official Action, and applicants believe the amendments put the claims in condition for allowance, or in better form for appeal.

Claims 7, 8, 9, 15, 16 and 21 stand rejected under 35 USC § 102(b) as being anticipated by von Behrens. Applicants have canceled claims 7, 8 and 16. Claims 9 and 15 are amended to depend from claim 1, and claim 21 is amended to state the container consists of the recited elements, and to state that the capillary walls are about 0.1 mm thick. The amendments to the claims are believed to obviate the 35 USC § 102(b) rejection based on the von Behrens reference.

Claim 11 stands rejected under 35 USC § 103(a) as being unpatentable over von Behrens. Claim 11 depends from claims 10. Claim 10 has been amended to depend from claim 1. Claim 1 specifies that the reaction portion of the claimed container is defined by a very thin wall, wherein the walls are composed of a material that exhibits a high level of thermal conductivity. The thickness and composition of the vessel walls represent factors

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relevant to the speed at which the contents of the vessel can be heated and cooled by an external differential in temperature. The von Behrens reference is silent regarding the thickness of the walls of the disclosed sample vessels and is devoid of any suggestion regarding the use of a thin walled capillary tube as a component of a sample container. Accordingly, claim 11 is believed to be patentable over the teachings of the von Behrens reference.

Claims 17 and 18 stand rejected under 35 USC § 103(a) as being unpatentable over by von Behrens in view of Gerarde (US 3,518,804). Claims 17 and 18 have been canceled rendering the rejection moot.

Claims 1-6 and 19 stand rejected under 35 USC § 103(a) as being unpatentable over Gerarde (US 3,518,804) in view of Gerarde (US 3,045,494).

Independent claims 1 and 21 have been amended to replace the transitional term "comprising" with "consisting of" to emphasize that the claimed vessels are **empty** vessels, and do not contain any sample material. This amendment is made to distinguish over prior art pipettes devices that are sealed after a liquid is taken up by the pipette.

The Gerarde '804 and '494 patents are directed to micropipettes for receiving a predetermined quantity of liquid and subsequently transferring the liquid from the capillary space into a storage chamber attached to the capillary tube. To function as micropipettes, the capillary tube of the Gerarde devices must be open at both ends of the tube. The Gerarde '804 reference suggests that the end of the reaction portion can be sealed, but this occurs only **after** a liquid sample has been retained by the micropipette device. At no time does either of the Gerarde references teach or suggest an empty container consisting of a receiving portion and a reaction portion, wherein the reaction portion consists of a capillary tube with a closed end. The amended claims specifically exclude the presence of a liquid sample in the container.

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Nor is it obvious to modify the devices disclosed in the Gerarde '804 and '494 patents to prepare the device of the present invention, since closing the end of the capillary tube prior to uptake of the liquid sample would render their devices incapable as functioning as micropipettes. It cannot be obvious to modify a device in a manner that destroys its function.

The claimed container of the present invention is not a pipette. It is a container that is filled by applying a sample to a receiving portion that is in fluidic communication with the close-ended capillary tube of the reaction portion. The sample container of the present invention has been designed to provide for the rapid and homogenous thermal cycling of the container contents. The ability to rapidly thermal cycle a sample allows one to conduct nucleic acid amplifications in a shorter length of time, and has been found to increase the yield and specificity of the polymerase chain reaction relative to prior art methods. Furthermore, the containers of the present invention have been designed to allow real time monitoring of the amplification reaction by monitoring fluorescent emitted from the end tip of the container. As demonstrated in Fig. 22A, detecting fluorescence emitted from the end tip of the sample vessel provides a 10 fold increase in signal intensity relative to detecting fluorescence emitted from the side of the container.

Accordingly, the claimed sample vessels of the present invention represent a unique combination of elements that allows for optimal rapid thermal cycling of a sample placed within the container. The motivation for combining these separate and distinct elements to form applicants' novel container derives from applicants' discovery of the beneficial results in yield and specificity (see data of Figs. 6, 7 and 9) produced by conducting rapid cycling PCR. The empty containers of the present invention, as amended herein, are believed to be patentable over the cited Gerarde reference, and withdrawal of that rejection is respectfully requested.

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Claims 7, 9-12, 15-18 and 20-22 stand rejected under 35 USC § 103(a) as being unpatentable over Gerarde (US 3,518,804) in view of Gerarde (US 3,045,494) taken in further view of Hawes. Claims 7, 16-18 and 22 have been canceled. Claims 9-12, 15, and 20 now depend from claim 1, and claim 21 has been amended to incorporate the same limitation as claim 1 regarding the thickness of the capillary tube wall. Accordingly, the amendments to the claims are believed to overcome the rejection of claims 9-12, 15, 20 and 21 for the reasons stated immediately above. Simply stated the Gerarde references fail to teach or suggest a sample container consisting of a receiving portion and a reaction portion, wherein the reaction portion consists of a capillary tube closed at one end. Nor do the cited references provide any motivation for preparing an empty container that has a receiving portion attached to a capillary tube, wherein the capillary tube has thin walls and a closed end.

In addition, with regards to claim 20, the Examiner contends that one of ordinary skill in the art would know to seal the end of a capillary tube of the primary reference for the known and expected result of providing an art recognized means of interfacing the end of the capillary tube with optical interrogation devices. However, applicants respectfully submit there is no motivation provided within the von Behrens or the Gerarde references that would direct one of ordinary skill to consider the optical characteristics of their devices. The references are devoid of any suggestion that their device could be used with optical interrogation devices. Accordingly, there is no motivation to combine the teaching of Hawes (relating to laser-excited raman spectrometers) with the teaching of the Gerarde references (which related to micropipettes). Furthermore, the suggested methods disclosed in Gerarde for sealing the end of the capillary tube appear to be inconsistent with allowing optimized optical transmissibility for light having a wavelength of about 400 nm to about 800 nm.

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Claims 9-12, 15, 20 and 21 as amended are believed to patentable over the cited references. Withdrawal of the rejection of claims 9-12, 15, 20 and 21 under 35 USC § 103(a) as being unpatentable over Gerarde (US 3,518,804) in view of Gerarde (US 3,045,494) taken in further view of Hawes is respectfully requested.

Claim 19 stands rejected under 35 USC § 112, first paragraph for failure to comply with the written description. Applicants respectfully traverse.

The Examiner contends that the specification fails to provide written support for a capillary tube having a wall thickness of about 0.1 mm and a diameter of other than an inner diameter of 0.8 mm. Applicants note that the specification is replete with references to the importance of "thin walled" capillary tubes. As noted at page 18, lines 4-7, "The response time for sample cooling [and heating] is very fast due to the use of thin walled glass capillary tubes for holding samples, ..." Each of the descriptions in the specification relating to the desirability of "thin walled" containers makes no reference to the diameter of the vessel. To require applicants' claims to be limited to a thin wall vessel only when the vessel has an inner diameter of 0.8 ignores applicant's clear intent, as disclosed in the present specification, that thin walled tubes a varying sizes can be used. See in particular, Example 1, page 21, lines 15-32, where applicants make clear that, "The thin walled capillary tubes 108 have several important advantages over previously used devices as described earlier... It is also preferred that the sample holding structure contain a volume anywhere from about 1 pl to about 10,000 ul but those skilled in the art will appreciate that other volumes of samples can be used within the scope of the present invention if the different thermal mass of the structure is considered." Thus the specification discloses that vessels of varying dimensions (necessary to accommodate the broad range of volumes), and all having "thin walls" were envisioned as part of the present invention.

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One would readily understand that the wall thickness and the inner diameter of the vessel are two independent elements of the vessel that can be varied to optimized thermal conductance. Rather than rely on the term "thin walled" applicants have merely substituted a more definitive numerical value for the term "thin walled." Applicants have clearly identified where the support for the numerical value for the wall thickness is found in the specification, and the substitution of this more specific limitation for the generic term "thin walled" is fully compliant with the written description requirement. Applicants respectfully request the withdrawal of the rejection of claim 19 under 35 USC § 112, first paragraph.

The foregoing claim amendments and remarks are believed to fully respond to the Examiner's rejections and the claims are believed to be in condition for allowance. Applicants respectfully request allowance of the claims, and passage of the application to issuance. If any further discussion of this matter would speed prosecution of this application, the Examiner is invited to call the undersigned at (434) 220-2866.

Respectfully submitted,



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